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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,909	12/18/2001	Heather L. Davis	C1039/7058(HCL X04/19/02)	8458
7590 06/24/2004			EXAMINER	
Helen C. Lockhart Wolf, Greenfield & Sacks, P.C. Federal Resrve Plaza 600 Atlantic Avenue Boston, MA 02210			PARKIN, JEFFREY S	
			ART UNIT	PAPER NUMBER
			1648	
DATE MAILED: 06/24/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/023,909

Applicant(s)

DAVIS ET AL.

Examiner

Jeffrey S. Parkin, Ph.D.

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-98 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,6,7,15-19,34 and 36-98 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,8-14,20-33 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Serial No.: 10/023,909
Applicants: Davis, H. L., et al.

Docket No.: C1039.70058
Filing Date: 12/18/01

Detailed Office Action

Status of the Claims

Applicants' election of Group II (claims 1, 4, 5, 8-14, 20-33, and 35), with traverse, is acknowledged. Because applicant did not distinctly and specifically point out the purported errors in the restriction requirement, the election has been treated as an election without traverse (refer to M.P.E.P. § 818.03(a)). Claims 2, 3, 6, 7, 15-19, 34, and 36-98 have been withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

35 U.S.C. § 120

Applicants are reminded that if priority under 35 U.S.C. § 120 based upon a previously filed copending application is desired, specific reference to the earlier filed application must be made in the instant application. **This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.** The status of non-provisional application(s) (whether patented or abandoned) should also be included. **If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application.** If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. If applicant desires priority based upon a National Stage filing, this information should also be referenced in the first sentence of the specification (i.e., This application is a National Stage entry of International Application No. PCT/CCPY/NNNNN, filed , 199N). It appears that U.S. Serial No. 09/325,193 has issued as U.S. Patent No. 6,406,705. The first paragraph of the specification should be amended to reflect this development.

37 C.F.R. § 1.98

The information disclosure statement filed 12 June, 2002, has been placed in the application file and the information referred to therein has been considered.

The information disclosure statement filed 09 February, 2004, fails to comply with 37 C.F.R. § 1.98(a)(1), which requires a list (i.e., PTO-1449) of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered.

Applicants are reminded that the listing of references in the specification (e.g., pp. 58-59) is not a proper information disclosure statement. 37 C.F.R. § 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and M.P.E.P. § 609 ¶ A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited or considered by the examiner on a form PTO-892 or PTO-1449, they have not been considered.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 8-14, 20-33, and 35 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are broadly directed toward methods

for the induction of antigen-specific immune responses in a subject through the administration of antigen and a combination of adjuvants comprising a CpG dinucleotide and non-nucleic acid adjuvant (e.g., MPL).

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the structural requirements of any given ISS-ODN. The skilled artisan would require a knowledge of those sequences that should be included in any given ISS prior to practicing the invention. However, the disclosure fails to provide sufficient guidance pertaining to the composition and length of those sequences that produce a synergistic immune response when combined with another adjuvant.

2) The disclosure fails to provide adequate guidance pertaining to those immune stimulating adjuvants (e.g., saponins, MPL, MDP, etc.) that can reasonably be expected to produce a synergistic immune response when combined with another adjuvant. The skilled artisan would need to know which combination of CpG-ODN and adjuvant should be employed, and which combination would reasonably be expected to provide a synergistic immune response. However, the disclosure is silent concerning this point.

3) The prior art is unpredictable and teaches that many putative

ISS elements do not function in the manner desired and often fail to facilitate immune responses to the immunogen of interest. Moreover, the skilled artisan cannot reasonably predict which combination of adjuvants will have a synergistic effect when employed concomitantly. The effectiveness of any given preparation will depend upon several factors including the antigen, adjuvants, dose, immunization regimen, and site of immunization. Because of the empirical nature of this process, the skilled artisan cannot reasonably predict which combinations of adjuvants will display synergistic effects when administered concomitantly with an immunogen. This is not surprising considering the complexity of the immune system.

4) The claims are of considerable breadth and are not fully supported by the disclosure. The broadest claims are not limited to any particular CpG-ODN or immune stimulating adjuvant or immunogen. Accordingly, the claims literally encompass tens-of-thousands of permutations. However, the disclosure fails to teach which combination(s) of immunogen, CpG-ODN, and adjuvant will produce the desired response.

5) The disclosure fails to provide a single working embodiment involving an immunogen, CpG-ODN, and immune stimulating adjuvant (e.g., saponin, MPL, LPS, MDP, etc.). A single example was provided in the disclosure involving a specific CpG-ODN, depo-effect inducing adjuvant (e.g., ALUM), and immunogen (e.g., HBsAg). However, alum is a depo-inducing adjuvant and is not covered by the current claim language. Thus, this example does not constitute a proper working embodiment.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

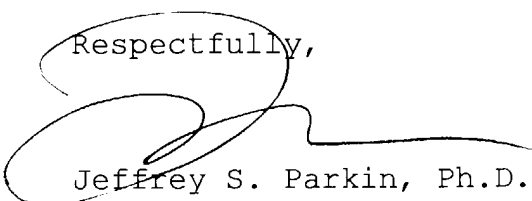
Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from

9:30 AM to 7:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (571) 272-0910 or (571) 272-0902, respectively. Direct general inquiries to the Technology Center 1600 receptionist at (571) 272-1600.

Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Respectfully,



Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

13 June, 2004